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Case Report

Meckel Gruber Syndrome in a Nigerian child: A Case Report and Review of the Literature.

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Abstract

Meckel-Gruber Syndrome (MGS) is a rare and lethal autosomal recessive disorder characterized by a triad of occipital encephalocele, polycystic kidneys, and polydactyly. The worldwide incidence varies from 1 in 13,250 to 1 in 140,000 live births, with a 25% reoccurrence rate. Prenatally, diagnosis can be made by ultrasonography for fetal anomalies at 11 to 14 weeks of pregnancy, which can guide management decisions. We report a female baby with the characteristic features of this syndrome, which was confirmed by autopsy findings.

Keywords: Meckel Gruber Syndrome; Encephalocele; Polycystic Kidneys; Polydactyly; Consanguinity.

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Introduction

Meckel-Gruber Syndrome (MGS), originally described by Meckel in 1822 and later by Gruber, is a rare and potentially fatal autosomal recessive disorder with a worldwide incidence of 1 in 13,250 to 140,000 live births. It is characterized by the triad of occipital meningo-encephalocele, polycystic kidneys, and post-axial polydactyly.[1–3] In addition, cardiac, hepatic, splenic, musculoskeletal, and genital anomalies are also linked to MGS, which has an estimated recurrence rate of 25%. The disease is lethal as affected infants are stillborn or die within hours to days of birth, with deaths probably related to severe central nervous system defects and/or renal defects.[3]

In this report, we present a female baby with the typical triad of Meckel-Gruber Syndrome. Parental consent was obtained, with written informed consent provided by the father, following ethical standards for the publication of this case report.

Case Report

We report the case of a term female neonate delivered via elective Caesarean section to a 25-year-old unbooked Para 4^{+0} A2 woman who was referred from a peripheral hospital on account of suspected encephalocele detected on ultrasound scan at term. The baby was apneic at birth with Apgar scores of 1 and 2 at 1 and 5 minutes, respectively, and weighed 3,087 grams. Cardiopulmonary resuscitation did not improve Apgar scores, and the baby was confirmed clinically dead at 45 minutes of life. Mother had no history of exposure to radiation or chemicals during pregnancy, nor took unprescribed medication. She was the 4^{th} born of her mother in a monogamous consanguineous family setting (parents were first cousins). A year before her conception, the mother was delivered of a stillbirth that had occipital encephalocele, swollen, flabby abdomen, and polydactyly, whose picture was shared by the parents (Figure 1). The other two siblings were alive and well.

Evident at birth were a ruptured occipital encephalocele, bilateral postaxial polysyndactyly of the upper and lower limbs, and a swollen, lax abdomen. Other gross anomalies observed included orofacial anomalies such as low-set ears, hypertelorism, cleft palate, ankyloglossia, a set of 20 natal teeth, and microphthalmia. Musculoskeletal anomalies included a short, webbed neck, arthrogryposis at the elbow and knee joints, and talipes varus (Figures 2 and 3).

The postmortem examination confirmed the presence of bilateral polycystic kidneys and other anomalies such as atrial septal defect, collapsed lungs, hepatic fibrosis, and cerebral oedema (figure 4). Histological examination of cut sections of both kidneys showed cystic spaces lined by single to multiple layers of flattened to cuboidal immature epithelium with occasional collarettes of immature mesenchyme, with corresponding multiple renal cysts on gross morphology. The sections from the liver showed hepatic fibrosis on gross morphology and areas of biliary duct hyperplasia and hepatic fibrosis on microscopical examination (Figure 5). The Parents were counseled on the chance of recurrence in subsequent pregnancies.

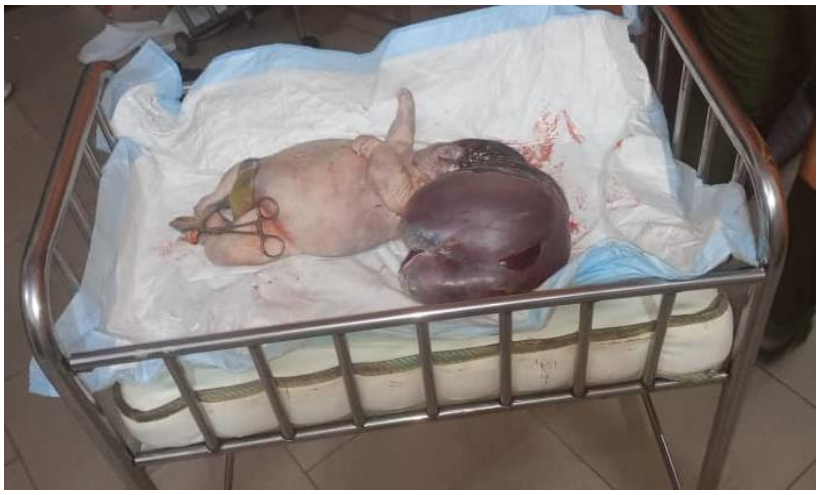

Figure 1: Preceding sibling delivered stillbirth with encephalocele, deformed limbs with extra digits, and abdominal swelling (Photo credit: parents)

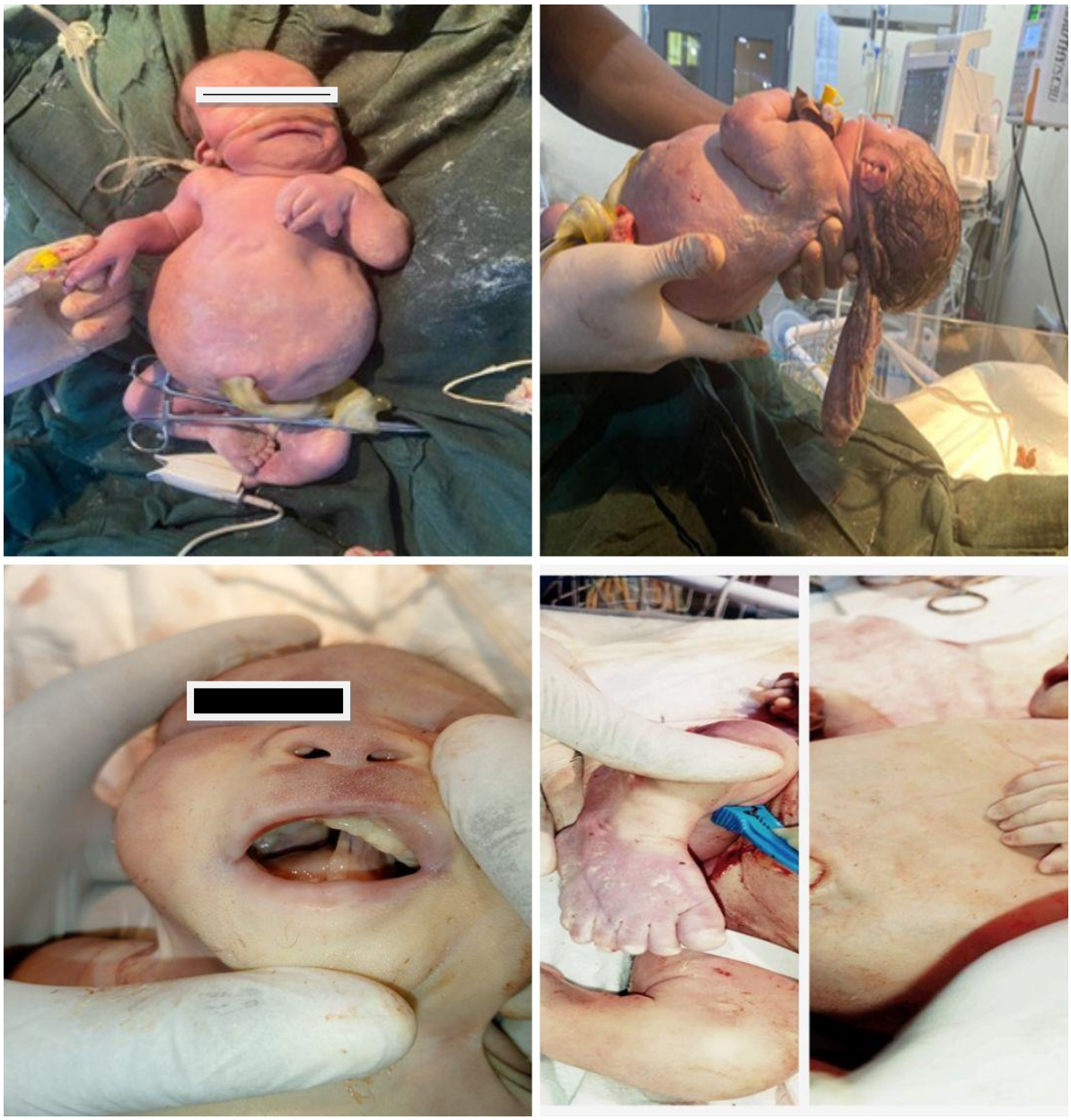

Figure 2: (A) Facial anomalies: hypertelorism, lowset ears; arthrogyroposis, talipes varus, polysyndactyly, swollen abdomen with flank fulness, (B) ruptured encephalocele, (C) natal teeth and cleft palate, (D) Post axial polysyndactyly

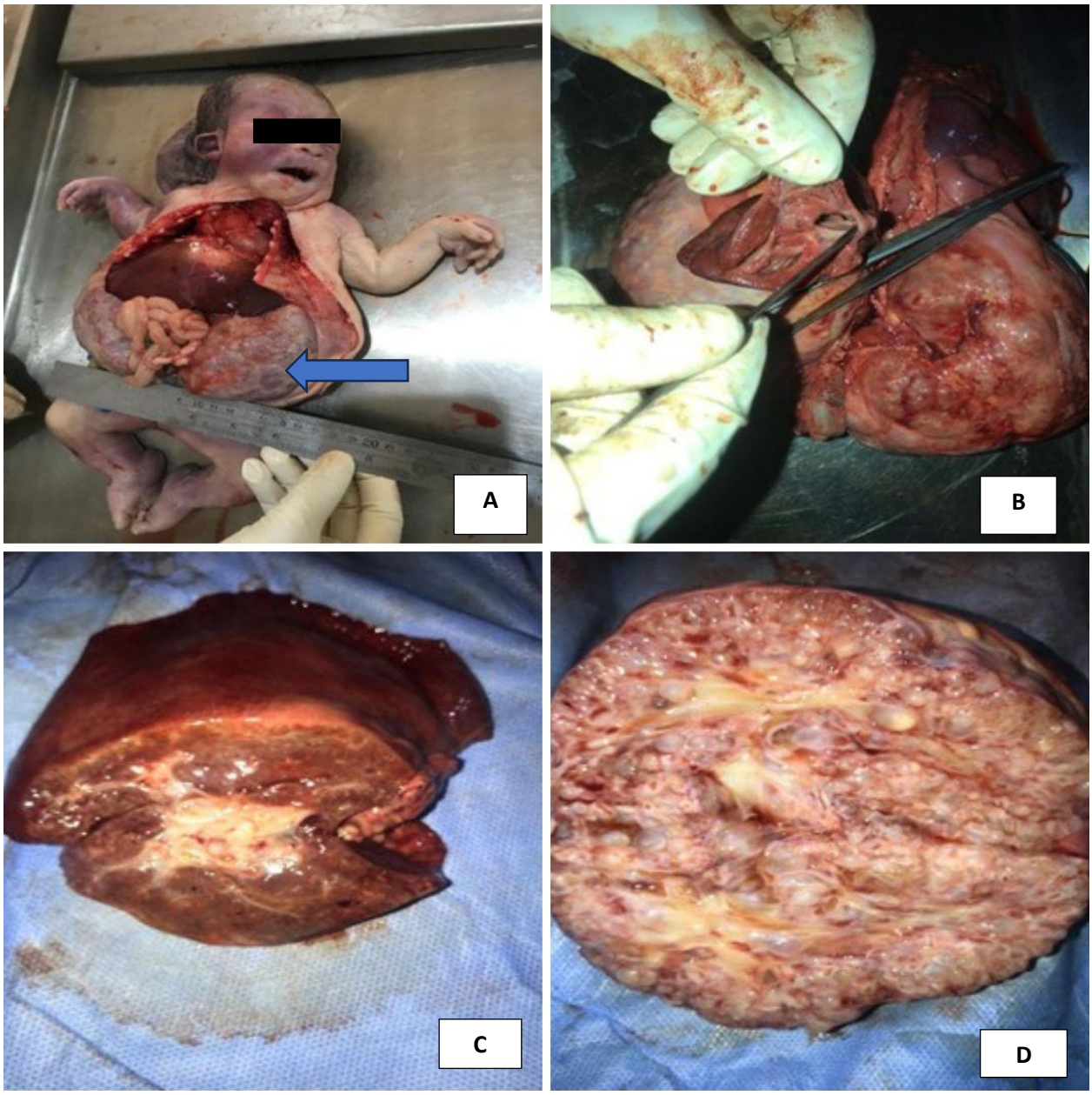

Figure 3: A) Bilateral polycystic kidneys (blue arrow) in the baby, B) atrial septal defect, C) Liver fibrosis, D) Polycystic kidney.

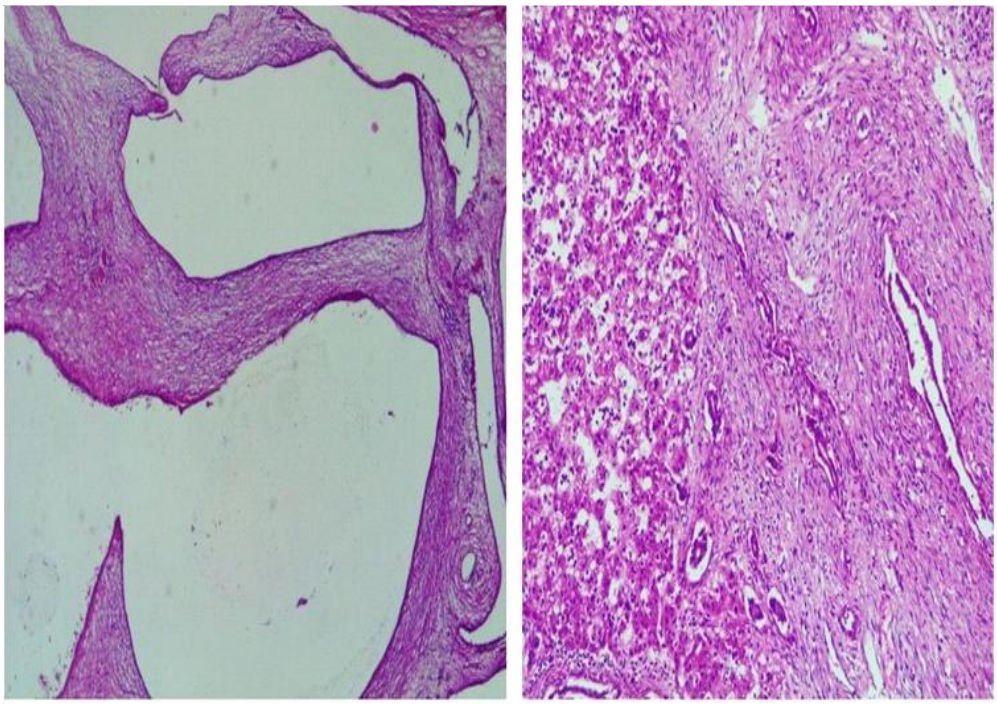

Figure 4: A). Photomicrograph from the section of kidneys shows cystic spaces lined with single to multiple layers of flattened to cuboidal immature epithelium with occasional collarettes of immature mesenchyme in the kidneys. B). Photomicrograph of the liver showing areas of biliary duct hyperplasia and hepatic fibrosis.

Discussion

Meckel-Gruber syndrome, characterized by a typical triad of cystic kidneys, occipital encephalocele, and post-axial polydactyly, is a congenital anomaly resulting from mutations that disrupt the structure or function of primary cilia involved in key developmental signaling pathways.[1–3] The disorder caused by mutations in ciliary genes is collectively referred to as ciliopathies, and Meckel-Gruber syndrome is the most severe form of this condition. It is a complex syndrome with extreme heterogeneity, with mutations identified in 14 genes.[4]

There is variability in the spectrum of clinical features among reported cases due to its variable expressivity; however, two of the three major anomalies are sufficient for a definitive diagnosis.[1,3] However, another author after review of series of cases and observed that cystic dysplasia of the kidneys with fibrosis of the liver is a constant finding in the "true" Meckel syndrome and therefore proposed that cystic dysplasia of the kidneys with fibrotic changes of the liver and occipital encephalocele or some other central nervous system malformation be considered as minimal diagnostic criteria of MGS.[5]In the present case, the baby had occipital encephalocele (Figure 2), post-axial polysyndactyly (Figure 3), and abdominal swelling with bilateral flank masses (Figure 2), which were confirmed to be bilateral polycystic kidneys on postmortem examination as well as fibrosis in the liver and biliary duct hyperplasia on histologic examination (Figure 4).

Features of MGS that have been reported in the literature, occurring occasionally (seen in 25–40% of cases), include limb deformity, male genital anomalies, microcephaly or anencephaly, cleft lip/palate, craniofacial defects, heart defects, and pulmonary hypoplasia.[5–7] While features rarely seen (in less than 20% of cases) include lung or thyroid cystic dysplasia, retinal colobomas, and situs abnormalities.[6,7] In addition to the major criteria diagnostic criteria (occipital encephalocele, post axial polysyndactyly and bilateral polycystic kidney), the index case had limb abnormalities- arthrogryposis at the elbow and knee joint and micromelia; craniofacial defects-low-set ears, hypertelorism, microphthalmia (Figure 2), and an atrial septal defect seen at postmortem examination (Figure 4B). Other features observed in the index case, which are rarely reported, include a set of natal teeth, ankyloglossia, and a short, webbed neck (Figure 2).

Meckel-Gruber syndrome is typically a lethal disorder, with most affected infants stillborn or dying shortly after birth due to the severity of the malformations.[5,6] The index case died shortly after birth, and the previous birth in the mother with similar physical features (occipital swelling, swollen abdomen, and extra digits in hands and feet) to the index case was stillborn (Figure 1). As an autosomal recessive condition with a 25% recurrence risk, it affects both genders equally, and consanguinity has been implicated as an important factor in the genetic basis of the disease.[8] In our case report, the parents are first cousins with a probable recurrence. A similar scenario was reported in a study in north central Nigeria, where parents who are in a consanguineous marriage had two consecutive births of babies with MGS; however, unlike the baby in our case, who died within an hour of birth, the second baby in their case report lived for a week.[9]

Prenatally, MGS can be detected through routine ultrasonography for fetal anomalies at 11 to 14 weeks of pregnancy, and termination of pregnancy is offered in some management guidelines.[8,10] In the index case, the anomaly was detected late, as the mother booked her pregnancy at 6 months of gestation at a peripheral hospital, and an ultrasound that revealed fetal anomaly (suspected encephalocele detected) was done at term, which necessitated her referral to our facility for delivery. An early antenatal ultrasound for screening of fetal anomaly, usually done at 11 to 14 weeks of gestation, allows for the planned management of some lethal fetal conditions that are not compatible with life. Pre-implantation genetic diagnosis can significantly reduce the risk of having a child with MGS by selecting unaffected embryos.[4] Pre-implantation genetic diagnosis provides an option for families to have children without the condition, reducing the emotional burden of such conditions. This, however, is expensive and not available in most developing countries.

Conclusion and Recommendation

Meckel Gruber syndrome is a lethal congenital disorder with increased recurrence risk, especially with consanguinity. Antenatal diagnosis can be made in the first trimester by ultrasound, which can inform management decisions. Where available, pre-implantation genetic diagnosis offers a valuable option for reducing recurrence and improving reproductive outcomes in affected families.

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